8. (Amended) A method for increasing the uptake of cytotoxic agents into a tumor comprising administering to a host having a tumor a composition comprising a PDGF aptamer and a cytotoxic agent, whereby the uptake of cytotoxic agents into the tumor is increased.

A3

REMARKS

The Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected Claims 1-11 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The second paragraph of Section 112 requires that the claims set out and circumscribe a particular area which applicants regard as their invention with a *reasonable* degree of precision and particularity.

Specifically, the Examiner finds that the claims are confusing in that the recited steps and elements "treating tumors," "reducing the interstitial pressure," "increasing the uptake of cytotoxic agents," "administering," "host" and PDGF-cytotoxic agent "composition" have no relationship to one another.

In response to this rejection, Claim 1 has been amended to provide a method for treating tumors comprising administering to a host having a tumor a therapeutically effective dose of a composition comprising a platelet-derived growth factor (PDGF) aptamer and a cytotoxic agent, whereby tumors are treated. Claim 5 has been amended to recite a method for reducing the interstitial fluid pressure (IFP) of a tumor comprising administering a PDGF aptamer. Claim 8 has been amended to recite a method for increasing the uptake of cytotoxic agents into a tumor comprising administering to a host having a tumor a composition comprising a PDGF aptamer and a cytotoxic agent, whereby the uptake of cytotoxic agents into the tumor is increased.

It is believed that the amendments are sufficient to overcome the rejection under 35 U.S.C. § 112, second paragraph. Reconsideration is respectfully requested.

The Rejection under 35 U.S.C. § 102(b)

The Examiner has rejected Claims 1, 2, 5, 6, 8, and 9 under 35 U.S.C. § 102(b) as being anticipated by the patent to Griffin, et al., U.S. Pat. No. 5,756,291. The Court of Appeals for the Federal Circuit has stated that anticipation requires the presence in a single prior art reference of each and every element of the claimed invention. *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed. Cir. 1984); *Alco Standard Corp. v. Tennessee Valley Auth.*, 1 U.S.P.Q.2d 1337, 1341 (Fed. Cir. 1986). "There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic v. Genentech Inc.*, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991) (citations omitted).

The Examiner asserts that Griffen, et al., disclose a PGDF aptamer and the method of identifying it wherein the aptamer comprises a composition comprising a cytotoxic agent; and that in therapeutic applications, the aptamer composition is administered to a host. The Examiner points out that the preamble to the claims has not been given weight in rejecting the claims because it is a recitation of a future intended use which is inherent in any prior art application and because there is not a relationship in the claims between the intended use, the host, and the administered composition.

Applicant notes that the claims have been amended as described above. The amendments to the claims provide a relationship between the intended use, the host and the administered composition.

The passages cited by the Examiner in Griffen, et al., do not describe every element of the subject claims. Griffen, et al., at the first cited passage (column 42, lines 1-5 and 24-44) suggests a PDGF aptamer. The second cited passage (column 12, lines 45-54) provides a suggestion of various auxiliary substances that may be coupled to aptamers. The third cited passage (column 38, lines 20-45) provides a generalized description of possible administration routes and formulations of aptamers for use in therapy.

Griffen, et al., does not teach a composition of a PDGF aptamer and a cytotoxic agent, nor does Griffen, et al. teach or suggest that PDGF aptamers can be used in the treatment of tumors, either alone, or in combination with a cytotoxic agent. Therefore,

Griffen, et al., does not teach a method of administering the composition to a patient with a tumor whereby tumors are treated, as required by Claims 1 and 2. Griffen, et al., also does not teach a method of administering a PDGF aptamer to a host having a tumor, whereby the interstitial fluid pressure of a tumor is reduced, as required by Claims 5 and 6. Finally, Griffen, et al., does not teach a method of administering a composition comprising a PDGF aptamer and a cytotoxic agent to a host having a tumor, whereby the whereby the uptake of cytotoxic agents into the tumor is increased, as required by Claim 8 and 9. Reconsideration is respectfully requested.

The Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 3, 4, 7, 10, and 11 under 35 U.S.C. § 103(a) as being unpatentable over the patent to Griffin, et al., U.S. Pat. No. 5,756,291 as applied to Claims 1, 2, 3, 6, 8, and 9 above and further in view of Kondratyev, U.S. Patent No. 5,502,037. The Examiner bears the burden of establishing a prima facie case of obviousness (Section 103). In determining obviousness, one must focus on Applicant's invention as a whole. *Symbol Technologies Inc. v. Opticon Inc.*, 19 U.S.P.Q.2d 1241, 1246 (Fed. Cir. 1991). The primary inquiry is:

> whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have had a reasonable likelihood of success . . . . Both the suggestion and the expectation of success must be found in the prior art, not in the applicant's disclosure.

In re Dow Chemical, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

Specifically, the Examiner asserts that:

> Regarding Claims 3, 7, and 10, drawn to an embodiment wherein the PDGF aptamer is SEQ ID NO:1, it would have been obvious and the skilled practitioner in the art at the time the claimed invention was made would have been motivated to use PDGF aptamers known in the art in the composition and in the administering method of Griffin, et al., based on preference, available materials and desired results in view of the known characteristics of substantial homology in sequence and similarity of structure, function, and target binding affinity in aptamers to the same specific target wherein the selected PDGF aptamers would have been expected to function in the same way as the claimed aptamers absent unexpected results.

The Examiner further asserts, regarding claims 4 and 11, drawn to an embodiment wherein the cytotoxic agent is selected from a group of chemotherapeutic agents known in the art, it would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to use a known chemotherapeutic agent in the PDGF composition of Griffen, et al, other than those taught by Griffin, e tal., based on preferences, available materials and cost considerations. Konratyev is cited as disclosing known cytotoxic agents including those of the claimed invention and those taught by Griffen, et al.

Applicant respectfully traverses this rejection. Claims 1, 5, and 8 have been amended as described above, and are not anticipated by Griffen, et al. for the reasons set forth in the preceding section. Rejected claims 3, 7, and 10, reciting SEQ ID NO:1, depend from Claims 1, 5, and 8, and therefore are not anticipated by Griffen, et al. for the same reasons. As Griffen, et al., neither teaches nor suggests the previously claimed methods, Applicant submits that Griffen, et al., can not obviate Claims 3, 7, and 10.

With regard to Claims 4 and 11, Applicant reiterates the arguments above regarding the lack of teaching or suggestion of the claimed methods in Griffen, et al.. The addition of Kondratyev does not remedy this deficiency. Kondratyev teaches covalent conjugates of peptides and cytotoxic agents. Kondratyev neither teaches nor suggests that non-peptide based homing agents can be used in the invention. The mere mention of additional cytotoxic agents in Kondratyev, when combined with Griffen, et al., is insufficient to obviate Claims 4 and 11. Reconsideration is respectfully requested.

Closing Remarks

Applicant believes that the pending claims are in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Respectfully submitted,

Date: December 11, 2002

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Marked up version showing changes to claims under 37 C.F.R. § 1.121(c)(ii)

1. (Amended) A method for treating tumors comprising administering to a host having a tumor a therapeutically effective dose of a composition comprising a platelet-derived growth factor (PDGF) aptamer and a cytotoxic agent, whereby tumors are treated.

5. (Amended) A method for reducing the interstitial fluid pressure (IFP) of a tumor comprising administering a PDGF aptamer to a host having a tumor, whereby the interstitial fluid pressure of a tumor is reduced.

8. (Amended) A method for increasing the uptake of cytotoxic agents into a tumor comprising administering to a host having a tumor a composition comprising a PDGF aptamer and a cytotoxic agent, whereby the uptake of cytotoxic agents into the tumor is increased.